

Hyperbilirubinemia in the Term Infant

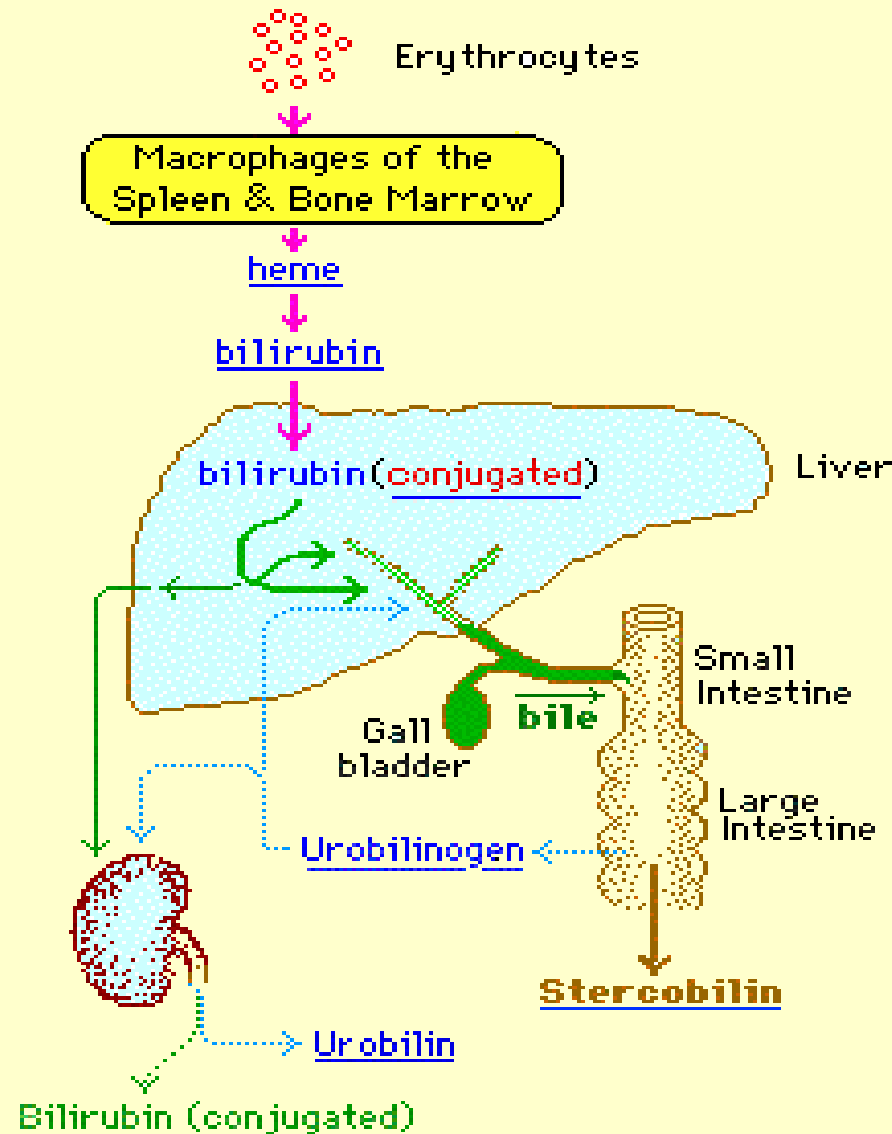
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Overview

- Neonatal Hyperbilirubinemia
- Bilirubin Production & Metabolism
- Risk Factors
- Etiologies
- Diagnosis
- Treatment
- Kernicterus
- Prevention

Neonatal Hyperbilirubinemia

- Definition = Total serum bilirubin (TSB) > 5 mg/dL
- Significance
 - Present in up to 60% of term newborns



Bilirubin Production & Metabolism

Risk Factors for Severe Hyperbilirubinemia

- Jaundice in 1st 24 hrs
- Visible jaundice prior to discharge
- Previous jaundiced infant
- Gestation 35-38wk
- Exclusive breastfeeding
- East Asian race
- Bruising, cephalohematoma
- Maternal age ≥ 25
- Male sex

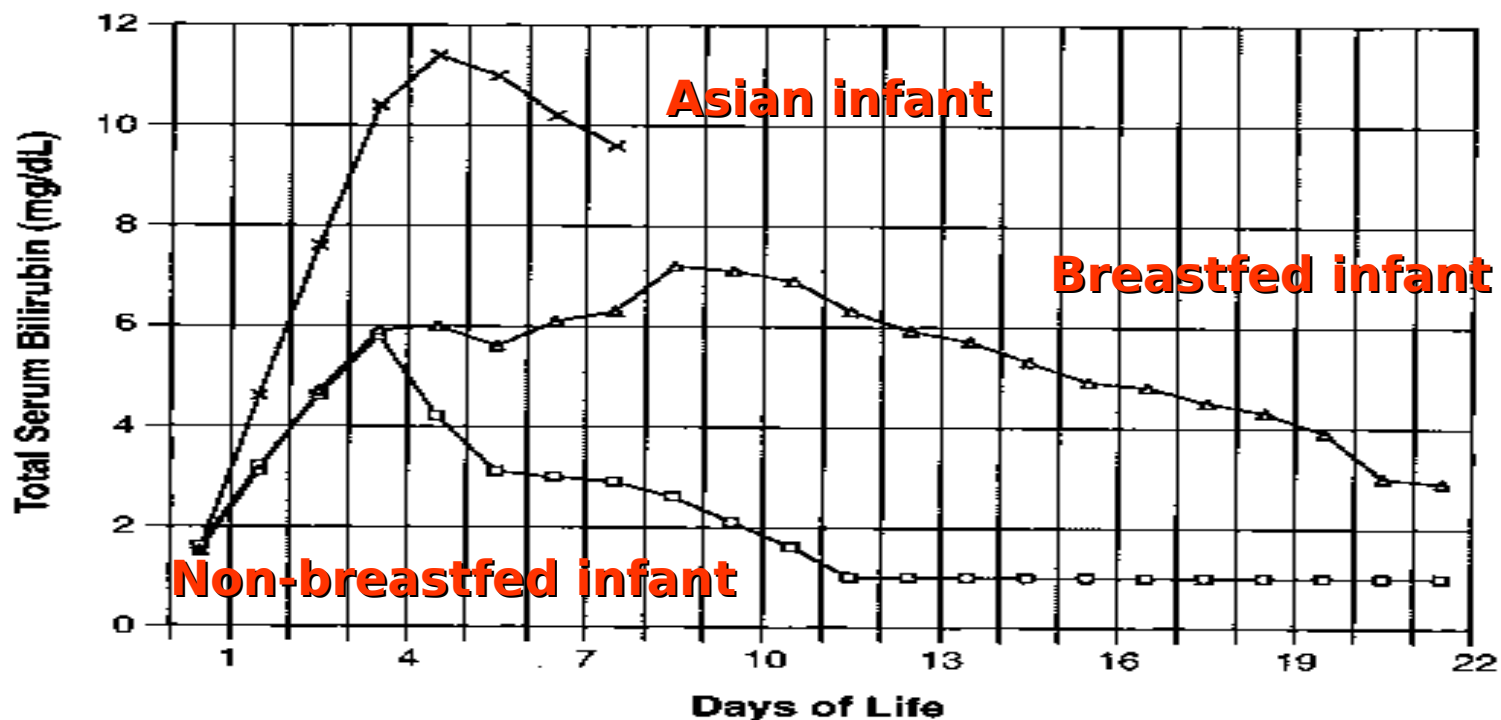
Etiologies

- Benign
 - Physiologic
 - Breast Milk
 - Breastfeeding
- Pathologic
 - Myriad of causes – more detail to come

Physiologic Jaundice

■ Features

- Elevated unconjugated bilirubin
- TSB generally peaks @ 5-6 mg/dL on day 3-4 and then declines to adult levels by day 10
 - Asian infants peak at higher values (10 mg/dL)
- Exaggerated physiologic (up to 17 mg/dL)



Physiologic Jaundice

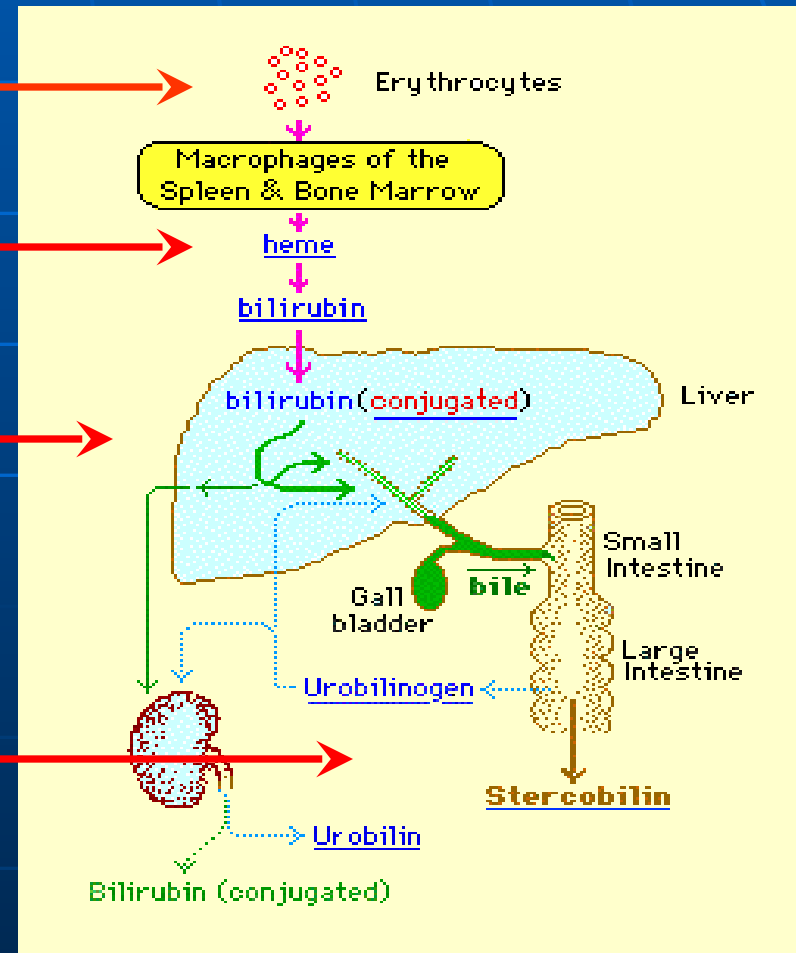
- Several factors responsible:

Increased rbc's

Shortened rbc lifespan

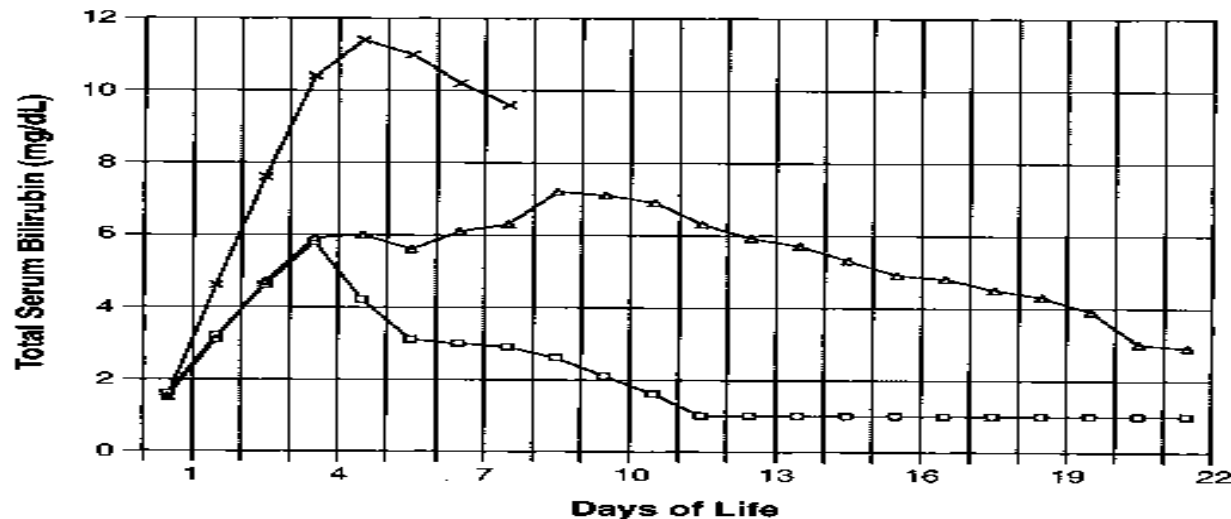
Immature hepatic uptake & conjugation

Increased enterohepatic Circulation



Breast Milk Jaundice

- Elevated unconjugated bilirubin
- Prolongation of physiologic jaundice
 - Slower decrease to adult levels of bilirubin
 - 66% of breastfed babies jaundiced into 3rd week of life
 - May persist up to 3 months
 - May be second peak @ day 10
- Average max TSB = 10-12 mg/dL
- TSB may reach 22-24 mg/dL
- ?Milk factor



Breastfeeding Jaundice

- Elevated unconjugated bilirubin
- Benign or pathologic
 - Elevated bilirubin in the 1st week of life tends to worsen breast milk jaundice during later weeks
- Equivalent to starvation jaundice in adults
- Mandates improved/increased breastfeeding
 - No water or dextrose supplementation
 - Formula OK

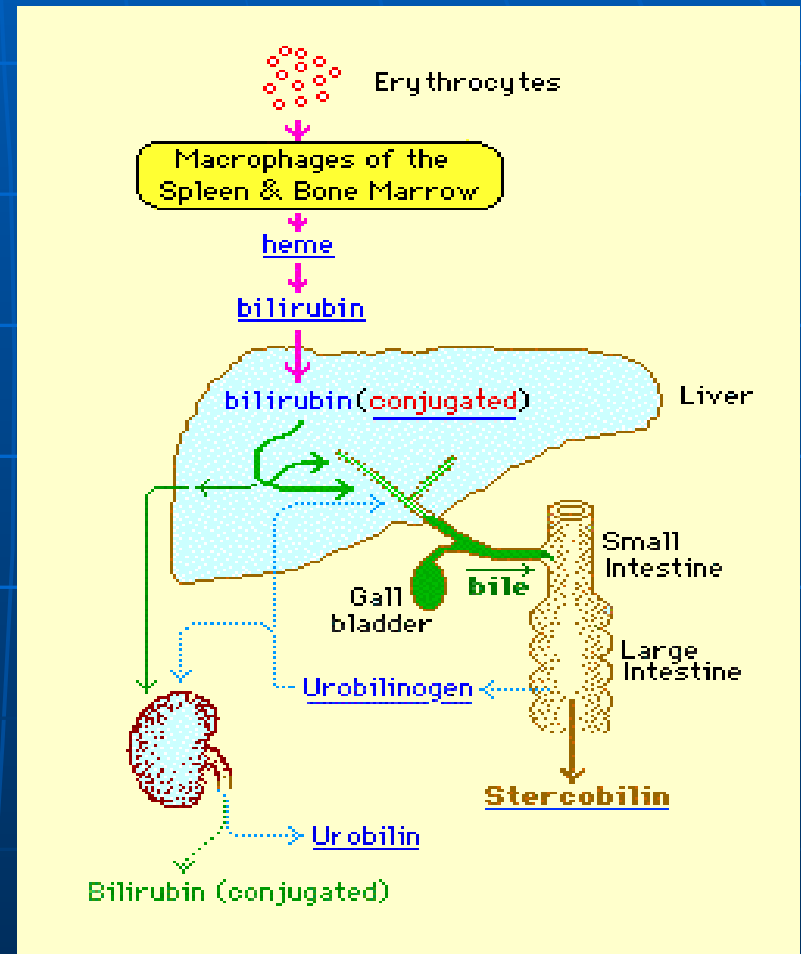
Pathologic Jaundice

■ Features

- Jaundice in 1st 24 hrs
- Rapidly rising TSB (> 5 mg/dL per day)
- TSB > 17 mg/dL

■ Categories

- Increased bilirubin load
- Decreased conjugation
- Impaired bilirubin excretion



Increased Bilirubin Load

- Elevated unconjugated bilirubin
- Hemolytic Disease
 - Features: elevated reticulocytes, decreased Hgb
 - Coomb's + Rh incompatibility, ABO incompatibility, minor antigens
 - Coomb's - G6PD, spherocytosis, etc.
- Non-hemolytic Disease
 - Features: normal reticulocytes
 - Extravascular sources – I.e. cephalohematoma
 - Polycythemia
 - Exaggerated enterohepatic circulation – I.e. CF

Decreased Bilirubin Conjugation

- Elevated unconjugated bilirubin
- Genetic Disorders
 - Crigler-Najjar
 - 2 types
 - Severe hyperbilirubinemia
 - Gilbert Syndrome
 - Mild hyperbilirubinemia
- Hypothyroidism

Impaired Bilirubin Excretion

- Elevated unconjugated and conjugated bilirubin (> 2 mg/dL or $> 20\%$ of TSB)
- Biliary Obstruction
 - Structural defects – I.e. biliary atresia
 - Genetic defects – Rotor's & Dubin-Johnson syndromes
- Infection – sepsis, TORCH
- Metabolic Disorders – I.e. α_1 antitrypsin deficiency
- Chromosomal Abnormalities – Turner's syndrome
- Drugs – I.e. ASA, sulfa, erythromycin

Diagnosis & Evaluation

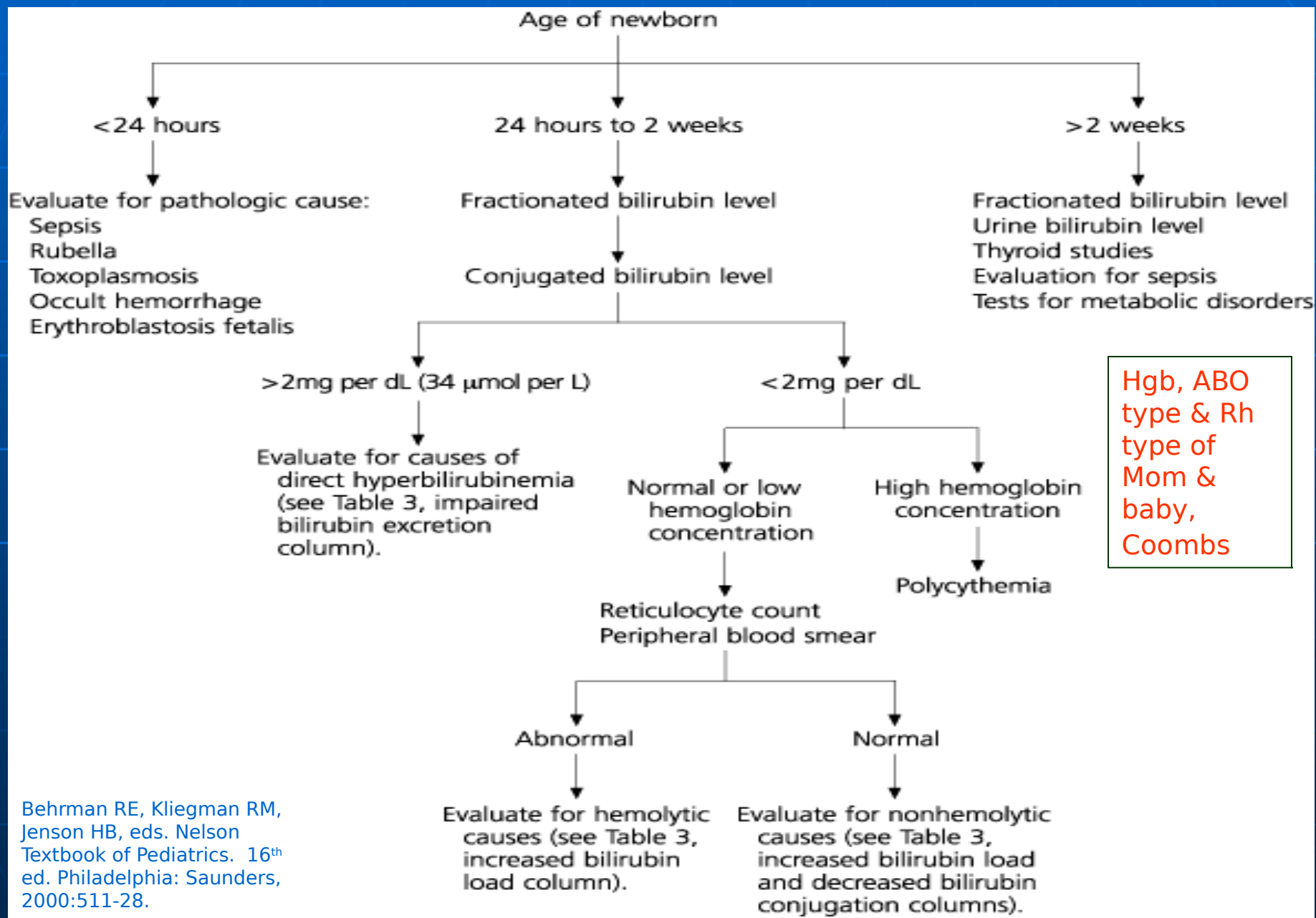
■ Physical Exam

- Jaundice visible when bilirubin reaches 5 mg/dL
- Milder jaundice generally confined to face & upper thorax
- Caudal progression generally signifies increasing bilirubin values

■ Laboratory

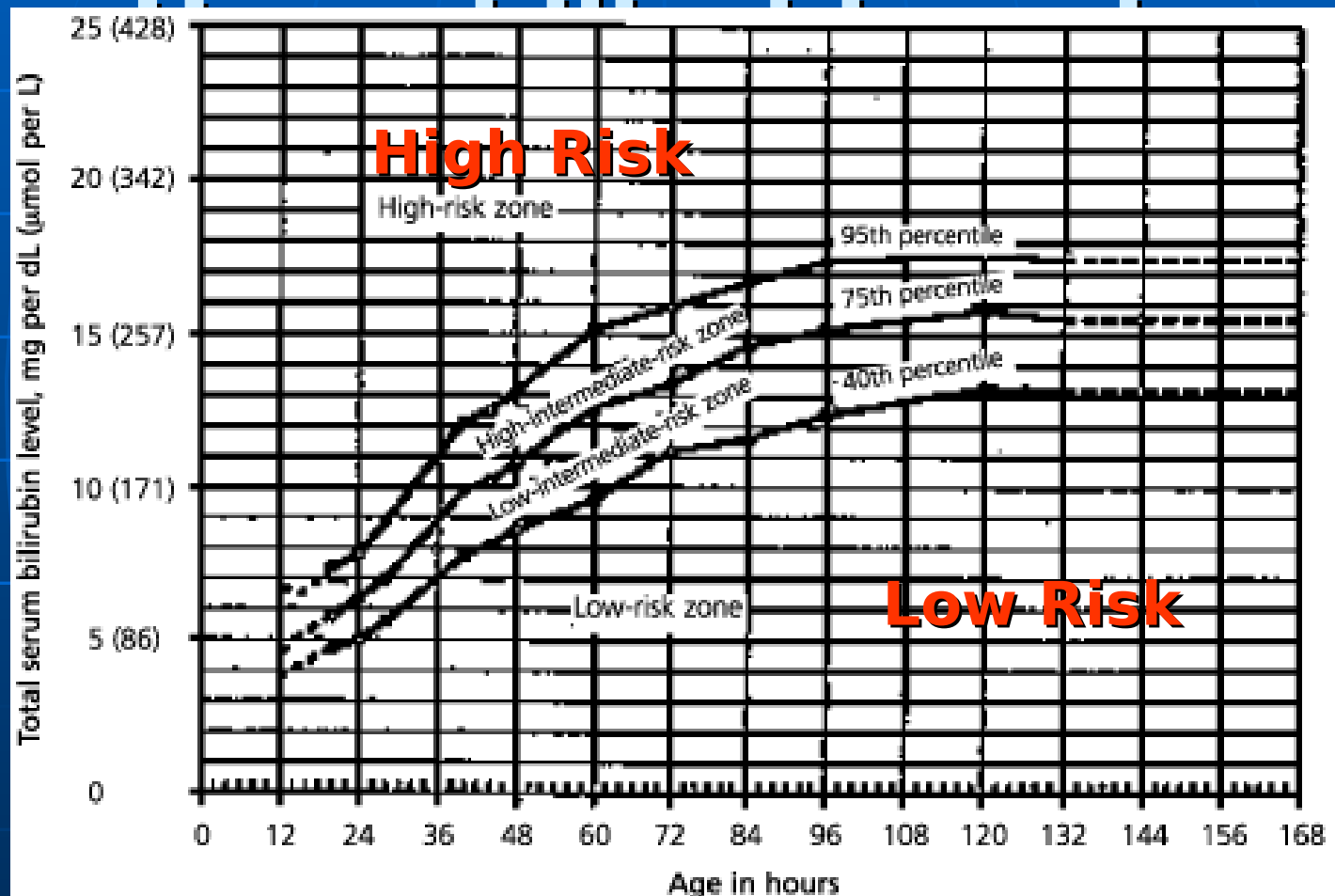
- Blood test
- Indirect measurements
 - Transcutaneous
 - Expired CO breath analyzer
 - One molecule of CO produced for every one molecule of Hgb produced from heme breakdown

Laboratory Evaluation of Term Newborn with Jaundice



Hgb, ABO
type & Rh
type of
Mom &
baby,
Coombs

Bilirubin Levels and Risk of Significant



*Bhutani VK, Johnson L, Sivieri EM. Predictive ability of a predischARGE hour-specific serum bilirubin for subsequent significant hyperbilirubinemia in healthy term and near-term newborns. *Pediatrics* 1999;103:6-14.

Management of Unconjugated Hyperbilirubinemia in the Term Newborn

Age (hr)	TSB Level (mg/dL)			
	Consider Phototherapy	Phototherapy	Exchange transfusion if phototherapy fails	Exchange transfusion and intensive phototherapy
≤24				
25-48	≥ 12	≥ 15	≥ 20	≥ 25
49-72	≥ 15	≥ 18	≥ 25	≥ 30
>72	≥ 17	≥ 20	≥ 25	≥ 30

Phototherapy

- Mechanism: converts bilirubin to water soluble form that is easily excreted
- Forms
 - Fluorescent lighting
 - Fiberoptic blankets
- Goal is to decrease TSB by 4-5 mg/dL or < 15 mg/dL total
- Breastfed infants are slower to recover
- Severe rebound hyperbilirubinemia is rare
 - Average increase is 1 mg/dL

Exchange Transfusion

- Mechanism: removes bilirubin and antibodies from circulation
- Most beneficial to infants with hemolysis
- Generally never used until after intensive phototherapy attempted

Kernicterus

- What is it?
 - Bilirubin induced toxicity to BG and brainstem nuclei
- Increase in cases beginning in early 1990's
 - At least partially related to early hospital discharge
- Multiple phases

Effects of Bilirubin Toxicity in Newborns

Early

Lethargy
Poor feeding
High-pitched cry
Hypotonia

Late

Irritability
Opisthotonos
Seizures
Apnea
Oculogyric crisis
Hypertonia
Fever

Chronic

Athetoid cerebral palsy
High-frequency hearing loss
Paralysis of upward gaze
Dental dysplasia
Mild mental retardation

Pilot Kernicterus Registry for Term & Near-Term (35-36wk)

Infants

- Retrospective data analysis of kernicterus cases in infants discharged as healthy
- Conducted by University of Pennsylvania
- Causes of kernicterus
 - Idiopathic – 32%
 - G6PD Deficiency – 32%
 - Bruising/Cephalohematoma – 10%
 - Infection – 7%
 - Crigler-Najjar syndrome – 3%

Prevention

- Lessons learned via Pilot Registry
 - Poor visual recognition of jaundice including estimation of its severity
 - Importance of interpreting TSB values in terms of age of infant
 - Early follow-up necessary even if jaundice not present
 - Must be familiar with idiopathic hyperbilirubinemia & G6PD deficiency
- Stricter adherence to 1994 AAP guidelines
 - Aggressive work-up of jaundice in 1st 24 hours of life
 - 2-3 day hospital f/u for all babies discharged prior to 48 hrs of life especially if < 38 wks gestation
- Better risk assessments
- Breastfeeding support
- New guidelines- ? Universal bili screening

QUESTIONS?